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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.68       1.68

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STRUCTURE FILE UPDATES:    5 JUN 2002  HIGHEST RN 426206-38-4
DICTIONARY FILE UPDATES:   5 JUN 2002  HIGHEST RN 426206-38-4

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

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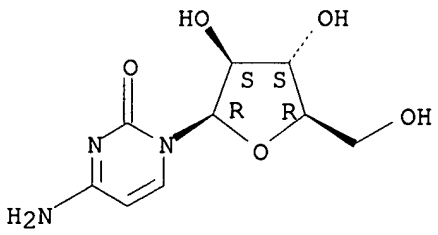
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s cytarabine
L1          17 CYTARABINE

=> d 17

L1   ANSWER 17 OF 17  REGISTRY  COPYRIGHT 2002 ACS
RN   69-74-9  REGISTRY
CN   2(1H)-Pyrimidinone, 4-amino-1-.beta.-D-arabinofuranosyl-,
     monohydrochloride (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Cytosine, 1-.beta.-D-arabinofuranosyl-, monohydrochloride (8CI)
OTHER NAMES:
CN   1-.beta.-D-Arabinofuranosylcytosine hydrochloride
CN   1-.beta.-D-Arabinofuranosylcytosine monohydrochloride
CN   Arabinofuranosylcytosine hydrochloride
CN   Arabinosylcytosine hydrochloride
CN   Aracytidine hydrochloride
CN   Cytarabine hydrochloride
CN   Cytosine arabinoside hydrochloride
CN   Spongocytidine-hydrochloride
CN   U 19920A
FS   STEREOSEARCH
MF   C9 H13 N3 O5 . Cl H
LC   STN Files:   ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS,
       CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB,
       IPA, NIOSHTIC, RTECS*, TOXCENTER, USAN, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
CRN  (147-94-4)

Absolute stereochemistry.
```

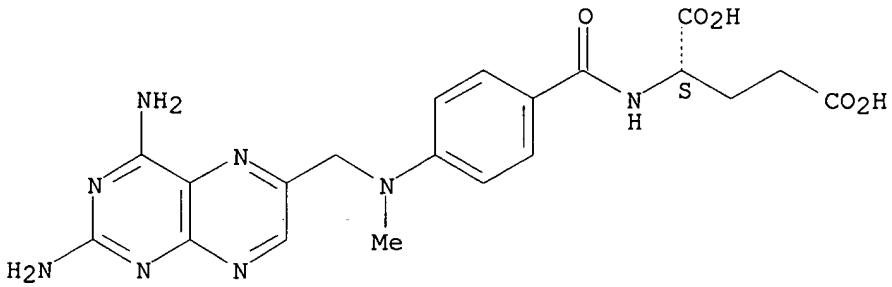


● HCl

105 REFERENCES IN FILE CA (1967 TO DATE)
105 REFERENCES IN FILE CAPLUS (1967 TO DATE)
13 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

2 ANSWER 97 OF 97 REGISTRY COPYRIGHT 2002 ACS
RN 59-05-2 REGISTRY
CN L-Glutamic acid, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, N-[p-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]-, L-(+)- (8CI)
OTHER NAMES:
CN (+)-Amethopterin
CN 4-Amino-10-methylfolic acid
CN 4-Amino-N10-methylfolic acid
CN 4-Amino-N10-methylpteroylglutamic acid
CN Amethopterin
CN Amethopterine
CN Antifolan
CN CL 14377
CN L-Amethopterin
CN **L-Methotrexate**
CN Methotrexat-Ebewe
CN **Methotrexate**
CN MTX
CN N-[p-[[2,4-Diamino-6-pteridinyl)methyl]methylamino]benzoyl]-L-(+)-glutamic acid
CN NSC 740
CN R 9985
FS STEREOSEARCH
MF C20 H22 N8 O5
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



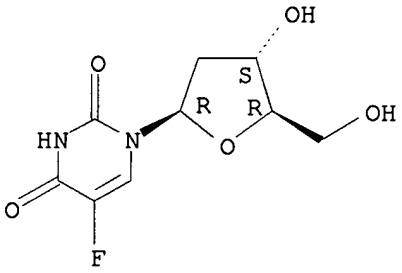
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9121 REFERENCES IN FILE CA (1967 TO DATE)
677 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9135 REFERENCES IN FILE CAPLUS (1967 TO DATE)
73 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

N 50-91-9 REGISTRY
CN Uridine, 2'-deoxy-5-fluoro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN **1-(2-Deoxy-.beta.-D-ribofuranosyl)-5-fluorouracil**
CN 2'-Deoxy-5-fluorouridine
CN 5-Fluoro-2'-deoxy-.beta.-uridine
CN 5-Fluoro-2'-deoxyuridine
CN 5-Fluorodeoxyuridine
CN **5-Fluorouracil 2'-deoxyriboside**
CN **5-Fluorouracil deoxyriboside**
CN FdUrd
CN Floxuridin
CN Floxuridine
CN FUDR
CN NSC 27640
FS STEREOSEARCH
DR 888-03-9, 3460-74-0
MF C9 H11 F N2 O5
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1725 REFERENCES IN FILE CA (1967 TO DATE)
56 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1725 REFERENCES IN FILE CAPLUS (1967 TO DATE)
34 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

CCESSION NUMBER: 1996:559918 CAPLUS
DOCUMENT NUMBER: 125:270670
TITLE: Alterations in chemical constituents of tea shoot during its development
AUTHOR(S): Yoshida, Yuko; Kiso, Masaaki; Nagashima, Hitoshi; Goto, Tetsuhisa
CORPORATE SOURCE: Tokyo Metrop. Agric. Exp. Stn., Tachikawa, 190, Japan
SOURCE: Chagyo Kenkyu Hokoku (1996), 83, 9-16
CODEN: CHKHB9; ISSN: 0366-6190
PUBLISHER: Nippon Chagyo Gijutsu Kyokai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The levels of the major chem. constituents in new shoots of **tea trees** were measured during their development. The 1st sprouts of 3 tea cultivars were analyzed from 1993 through 1995 for total nitrogen, caffeine, tannin, L-ascorbic acid, (-)-epicatechin (EC), (-)-**epicatechin gallate** (ECg) (-)-epigallocatechin (EGC), (-)-**epigallocatechin gallate** (EGCg) and (+)-catechin. Total nitrogen, caffeine and tannin decreased during the growth of new shoots. L-Ascorbic acid also tended to decrease with the shoot growth, but notably decreased after rainfalls irresp. of the cultivar, and levels restored after successive sunny days. During the early growth stage, the levels of EC and EGC were slightly increased. However, the levels of ECg, EGCg and catechin were significantly lower as the new shoots developed.

IT Plant growth and development
Tea (Camellia sinensis)
(chem. constituents of tea shoots during development)

IT Phenols, biological studies
Tannins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(chem. constituents of tea shoots during development)

IT 50-81-7, L-Ascorbic acid, biological studies 58-08-2, Caffeine, biological studies 154-23-4, (+)-Catechin 490-46-0, (-)-Epicatechin 970-74-1, (-)-Epigallocatechin **989-51-5**, (-)-**Epigallocatechin gallate 1257-08-5**
7727-37-9, Nitrogen, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(chem. constituents of tea shoots during development)

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:450109 CAPLUS
DOCUMENT NUMBER: 121:50109
TITLE: Tannin-metal(III) ion complexes, their preparation, and their pharmaceutical use
INVENTOR(S): Kiesgen de Richter, Renaud; Maurel, Jean Claude
PATENT ASSIGNEE(S): I.R.2.M. Societe en Nom Collectif, Fr.
SOURCE: Fr. Demande, 41 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2695390	A1	19940311	FR 1992-10770	19920909
FR 2695390	B1	19941125		
WO 9406809	A2	19940331	WO 1993-FR863	19930909
WO 9406809	A3	19940428		

W: CA, JP, RU, UA, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 659189 A1 19950628 EP 1993-919434 19930909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: FR 1992-10770 19920909
WO 1993-FR863 19930909

AB Complexes of metal(III) ions with a tannin or tannin mixt. are prepd. and used for treatment of diabetes and complications assocd. with this disease. A large no. of V(III) complexes with tannin-contg. exts. of various plants, or with specific tannins, were prepd. and tested for hypoglycemic activity in diabetic rats.

IT Maple
Witch hazel
(complexes with vanadium, for diabetes treatment)

IT Tannins
RL: BIOL (Biological study)
(complexes, with vanadium(III), for diabetes treatment)

IT Antidiabetics and Hypoglycemics
(tannin-metal(III) complexes as)

IT Inflammation inhibitors
(tannin-metal(III) ion complexes)

IT Acacia
Alfalfa
Eucalyptus globulus
Ginkgo biloba
Grape
Gymnema sylvestre
Nettle
Sage
Tea (Camellia sinensis)
Vaccinium myrtillus
(tannins, complexes with vanadium(III), for diabetes treatment)

IT Pine
(P. pinaster, tannins, complexes with vanadium(III), for diabetes treatment)

IT Currant (Ribes)
(R. nigrum, tannins, complexes with vanadium(III), for diabetes treatment)

IT Tannins
RL: BIOL (Biological study)
(complexes, with metal(III) ions, for treatment of diabetes)

IT Tannins
RL: BIOL (Biological study)
(mixts., complexes, with metal(III) ions, for treatment of diabetes)

IT 149-91-7D, Gallic acid, dimetagalloyl derivs.,complexes with vanadium(III)
327-97-9D, Chlorogenic acid, complexes with vanadium(III)
989-51-5D, Epigallocatechin gallate, complexes with vanadium(III) 4670-05-7D, Theaflavine, complexes with vanadium(III) 5127-64-0D, **Gallocatechin** gallate, complexes with vanadium(III) 7429-90-5D, Aluminum, complexes with tannins 7439-96-5D, Manganese, complexes with tannins 7439-98-7D, Molybdenum, complexes with tannins 7440-05-3D, Palladium, complexes with tannins 7440-06-4D, Platinum, complexes with tannins 7440-18-8D, Ruthenium, complexes with tannins 7440-31-5D, Tin, complexes with tannins 7440-32-6D, Titanium, complexes with tannins 7440-33-7D, Tungsten, complexes with tannins 7440-36-0D, Antimony, complexes with tannins 7440-47-3D, Chromium, complexes with tannins 7440-48-4D, Cobalt, complexes with tannins 7440-55-3D, Gallium, complexes with tannins 7440-56-4D, Germanium, complexes with tannins 7440-57-5D, Gold, complexes with tannins 7440-62-2D, Vanadium, complexes with tannins 7782-49-2D, Selenium, complexes with tannins 10028-14-5D, Nobelium, complexes with tannins 20283-92-5D, Rosmarinic acid, complexes with vanadium(III) 23567-23-9D, Procyanidin B3, complexes with vanadium(III) 28831-65-4D, Lithospermic acid, complexes

with vanadium(III) 29106-49-8D, Procyanidin B2, complexes with vanadium(III) 30964-13-7D, Cynarine, complexes with vanadium(III) 37064-30-5D, Procyanidin C1, complexes with vanadium(III) 37064-31-6D, Procyanidin C2, complexes with vanadium(III) 38713-01-8D, complexes with vanadium(III) 50678-27-8D, Pentagalloylglucose, complexes with vanadium(III) 94855-05-7D, Tara tannin, complexes with vanadium(III) 109008-78-8D, complexes with vanadium(III) 129159-07-5D, complexes with vanadium(III)
RL: BIOL (Biological study)
(for diabetes treatment)

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Small Molecule Drug Metabolism

by

Walter Yu
Celera Corporation

Published 15 April 2002

Table of Contents

I. Why are drugs metabolized?

Small molecule drugs are xenobiotics, foreign molecules, that the human **body**

attempts to deal with through a number of responses. Some drugs are excreted from the human body intact. Most drugs, however, need to be modified structurally to facilitate excretion. These modification processes are called drug metabolism. Drug metabolism is a detoxification function the human body possesses to defend itself from environment hostility. When a person is sick, however, the body needs some kind of medication to fight the disease. Ideally, a drug should reach the site of action intact, cure the disease, and leave the body after it completes its mission. However, drug developers often face the dilemma that a potential drug is either metabolized/excreted from the body too fast, that the drug can not reach its therapeutic effect, or too slow, that it stays in the body for a long time, causing side effects. (Remember the drug is a xenobiotic that the normal human body doesn't need.) The study of drug metabolism, therefore, serves primarily two purposes: to elucidate the function and fate of the drug, and to manipulate the metabolic process of a potential drug.

II. Where does metabolism occur in the body?

The liver is the primary site for metabolism. Liver contains the necessary enzymes for metabolism of drugs and other xenobiotics. These enzymes induce two metabolism pathways: Phase I (functionalization reactions) and Phase II (biosynthetic reactions) metabolism. Some typical examples of Phase I metabolism include oxidation and hydrolysis. The enzymes involved in Phase I reactions are primarily located in the endoplasmic reticulum of the liver cell, they are called microsomal enzymes. Phase II metabolism involves the introduction of a hydrophilic endogenous species, such as glucuronic acid or sulfate, to the drug molecule. Enzymes involved in phase II reactions are mainly located in the cytosol, except glucuronidation enzyme, which is also a microsomal enzyme.

Drugs are usually lipophilic substances (Oil-like) so they can pass plasma membranes and reach the site of action. Drug metabolism is basically a process that introduces hydrophilic functionailities onto the drug molecule to facilitate excretion. When the drug molecule is oxidized, hydrolyzed, or covalently attached to a hydrophilic species, the whole molecule becomes more hydrophilic, and is excreted more easily. Drugs often undergo both Phase I and II reactions before excretion. The Phase I reaction introduces a functional group such as a hydroxyl group onto the molecule, or exposes a preexisting functional group, and Phase II reaction connects this functional group to the endogenous species such as a glucuronic acid. The modified drug molecule may then be hydrophilic enough to be excreted.

Although liver is the primary site for metabolism, virtually all tissue cells have some metabolic activities. Other organs having significant metabolic activities include the gastrointestinal tract, kidneys, and lungs. When a drug is administrated orally, it undergoes metabolism in the GI track and the liver before reaching systemic circulation. This process is called first-pass metabolism. First-pass metabolism limits the oral bioavailability of drugs, sometimes significantly.

III. What happens to drugs once they are metabolized?

Drugs are ultimately excreted from the **body** through various routes. The kidney is the major organ for drug excretion. It excretes hydrophilic drug and drug metabolites through glomerular filtration. Macromolecules such as proteins are retained. Lipophilic drug molecules are not directly excreted from the kidney. Only after they are metabolized into more hydrophilic molecules, can they be excreted through the kidneys into the urine. Drugs and their metabolites are also excreted into bile. This is usually mediated by protein transporters. Drugs and their metabolites in bile are eventually released into the intestinal tract. The drugs may be reabsorbed into the **body** from the intestine. Drug metabolites such as glucuronide conjugates, may be converted back to the parent drug in the intestine through glucuronidase enzyme, and then reabsorbed into systemic circulation. This drug recycling process is called enterohepatic recycling. This process, if extensive, may prolong the half-life of the drug. The bile drugs and drug metabolites, if not reabsorbed by intestine, are excreted from the **body** through feces. Also, a variety of orally administrated drugs are excreted through feces because they are not absorbed through the intestine. Oral **bioavailability** constitutes a major challenge for drug developers. Other routes of excretion, such as sweat, tears, and saliva, are quantitatively less important. Excretion through breast milk is not important to the mother, but may be of key importance to the baby, because the drug may be toxic to the baby. Pulmonary excretion is important for anesthetic gases and vapor drugs.

IV. Are there common motifs (consensus sites) on molecules where metabolism occurs?

As is pointed out, small molecule drugs are usually lipophilic substances that can penetrate cell membranes to reach the site of action, and drug metabolism is a process of introducing hydrophilic functional groups onto the drug molecule. The most common phase I reactions are oxidative processes that involve cytochrome P450 enzymes. These enzymes are a super family of proteins found in all living organisms. These enzymes catalyze the following reactions: aromatic hydroxylation; aliphatic hydroxylation; N-, O-, and S-dealkylation; N-hydroxylation; N-**oxidation**; sulfoxidation; deamination; and dehalogenation.

These enzymes are also involved in a number of reductive reactions, generally under oxygen-deficiency condition. Hydrolysis is also observed for a wide variety of drugs. The enzymes involved in hydrolysis are esterases, amidases, and proteases. These reactions generate hydroxyl or amine groups, which are suitable for phase II conjugation.

Phase II conjugation introduces hydrophilic functionalities such as glucuronic acid, sulfate, glycine, or acetyl group onto the drug or drug metabolite molecules. These reactions are catalyzed by a group of enzymes called transferases. Most trasferases are located in cytosol, except the one facilitates glucuronidation, which is a microsomal enzyme. This enzyme, called uridine diphosphate glucuronosyltransferase (UGTs), catalyzes the most important phase II reaction: glucuronidation. Glucuronic acid contains a number of hydroxyl groups and one carboxylic acid functionality. This molecule is extremely hydrophilic, and improves the hydrophilicity of a drug molecule when they are covalently bound.

The following is a partial list of common metabolism motifs :

1. Aliphatic/Aromatic carbons: hydroxylation.
2. Methoxyl/methylamine group: demethylation.
3. Amine: N-**oxidation**, or deamination.
4. Sulfur: S-**oxidation**.
5. Phenol/alcohol: glucuronidation/sulphation.
6. Esters/amides: hydrolysis.

V. The top changes that occur and their mass shifts

Below is a brief list of mass shifts caused by metabolism of common functional groups.

1. Glucuronidation: plus 176 u.
2. Sulfation: plus 80 u.
3. **Oxidation** (N-, S-): plus 16 u.
4. Hydroxylation (aliphatic, aromatic): plus 16 u (or 32, if two sites).
5. Dealkylation: minus the alkyl group: minus 14 u for a methyl group, and 28 u for an ethyl group.
6. Hydrolysis: minus R-1 for ester hydrolysis into the acid.

VI. Conclusion

In reality, drug metabolism is an extremely complicated process, and the picture can be very messy. Often, a drug is metabolized into many products, some major, others minor. A complete picture of the metabolism of a drug is, in many cases, not possible, and not usually necessary.

VII. Resources

Articles

Raucy J L, Allen S W. Recent advances in P450 research. Pharmacogenomics J. 2001;1(3):178-86. Review.

Jaeschke H, Gores GJ, Cederbaum AI, Hinson JA, Pessayre D, Lemasters JJ., Mechanisms of hepatotoxicity. Toxicol Sci. 2002 Feb;65(2):166-76. Review.

Langowski J, Long A., Computer systems for the prediction of xenobiotic metabolism. Adv Drug Deliv Rev. 2002 Mar 31;54(3):407-15.

Roden D M., Principles in pharmacogenetics. Epilepsia. 2001;42 Suppl 5:44-8.

Herrlinger C, Klotz U. Drug metabolism and drug interactions in the elderly. Best Pract Res Clin Gastroenterol. 2001 Dec;15(6):897-918. Review.

Web Resources:

Michael Ivery's Metabolism Lectures School of Pharmacy, The University of Sydney, Australia. Eight great metabolism lectures in .ppt format.

The UK Drug Metabolism Group web site

Delaware Valley Drug Metabolism Discussion Group

Cytochrome P450 Drug Interaction Table, at Indiana University Department of Medicine

Journals:

Drug Metabolism and Disposition a publication of the American Society for Pharmacology and Experimental Therapeutics. They provide full length articles for download.

Current Drug Metabolism, Bentham Science Publishers Ltd.

ACCESSION NUMBER: 1995:294300 CAPLUS
DOCUMENT NUMBER: 122:54703
TITLE: Lipid-soluble green tea catechin antioxidant **solutions**
INVENTOR(S): Todd, Paul H., Jr.
PATENT ASSIGNEE(S): Kalamazoo Holdings, Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9422321	A1	19941013	WO 1994-US3494	19940331
W: CA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2159465	AA	19941013	CA 1994-2159465	19940331
EP 692934	A1	19960124	EP 1994-913988	19940331
R: CH, DE, GB, IE, LI				
US 5527552	A	19960618	US 1994-352439	19941209
PRIORITY APPLN. INFO.:			US 1993-41494	19930401
			WO 1994-US3494	19940331

AB Green tea catechins are made into **solns.** in a nonionic edible fat-sol. solvent; these **solns.** are effective antioxidants in fats, oil, foods, and ingredients of foods without imparting undesirable flavors, aromas, and ppts. Because tea polyphenols have **pos.** effects on human health, the resulting stabilized lipids can be considered to have nutritional qualities superior to the same lipid stabilized with common synthetic antioxidants. Unexpectedly strong **synergistic** effects with other natural antioxidants and with phosphates are also shown. Thus, 100 g of green tea was extd. with MeOH, enough water was added to keep the mass **liq.**, MeOH was evapd. at <80.degree. to give a thick **liq.** ext., 90 mL of hexane was added, the mixt. was agitated, the hexane phase was sepd. from the water phase, and the water phase was extd. again with 30 mL of hexane. After sepn. of the hexane phase, 10 g NaCl was added to the water layer and the pH adjusted to 3.5 with H3PO4, and the aq. phase was extd. twice with 150 mL EtOAc. The EtOAc was evapd. at <80.degree. to yield a dry catechin-rich fraction weighing 14.7 g. This powder was added to a C12 fatty alc., warmed, and agitated to give a 2.7% wt./wt. **soln.** When added at 0.3% wt./wt. (80 ppm catechin), the **soln.** was powerful in inhibiting oxidn. of fats and oils, the Rancimat ratios of induction time of the test sample to the control being 4.68 and 5.05 for coconut oil and chicken fat, resp.

CESSION NUMBER: 2001:208502 USPATFULL
TITLE: Composition and method for inhibiting **oral** bacteria
INVENTOR(S): Zhou, James H., 32 Hallmark Dr., Wallingford, CT, United States 06492

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6319523	B1	20011120	
APPLICATION INFO.:	US 2000-606294		20000629	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lilling, Herbert J.
LEGAL REPRESENTATIVE: Bachman & LaPointe, P.C.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 396
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A composition for inhibiting **oral** bacteria, including a polyphenol derivative composition; and at least one composition selected from the group consisting of mogroside derivative composition, licorice extract and **combinations** thereof, wherein the composition is effective to inhibit growth of **oral** microbials.

CCESSION NUMBER: 2001:173189 USPATFULL
TITLE: Effervescent green tea extract formulation
INVENTOR(S): Xiong, Weihong, Salt Lake City, UT, United States
Quan, Danyi, Salt Lake City, UT, United States
Patel, Dinesh C., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): XEL Herbaceuticals, Inc., Salt Lake City, UT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6299925	B1	20011009	
APPLICATION INFO.:	US 1999-342787		19990629	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Weier, Anthony J.
LEGAL REPRESENTATIVE: Thorpe North & Western, LLP
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
LINE COUNT: 619
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A solid state water soluble formulation in granular or **tablet** form is provided. The formulation is a natural products formulation containing a green tea plant extract in **combination** with other ingredients which create an effervescent **liquid** composition upon dispensing the formulation in a **liquid**. The **liquid** form of administration, as well as the effervescent properties of the dissolved formulation increase bioavailability of the advantageous components of the green tea plants such as Polyphenols, by increasing absorption speed and amount in the human body. The formulation may include additional components such as, other plant extracts, vitamins, ionic minerals, and other substances purported to be of a health benefit.

L6 ANSWER 4 OF 206 USPATFULL

ACCESSION NUMBER:	2002:314424 USPATFULL
TITLE:	Tea catechins as cancer specific proliferation inhibitors
INVENTOR(S):	Morre, Dorothy M., West Lafayette, IN, UNITED STATES Morre, D. James, West Lafayette, IN, UNITED STATES
PATENT ASSIGNEE(S):	Purdue Research Foundation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002176897	A1	20021128
APPLICATION INFO.:	US 2002-102502	A1	20020319 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-537211, filed on 29 Mar 2000, GRANTED, Pat. No. US 6410061		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-126893P	19990330 (60)
	US 1999-151109P	19990827 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711
NUMBER OF CLAIMS:	75
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	20 Drawing Page(s)
LINE COUNT:	1923

AB The invention described herein encompasses a methods and compositions of treating cancer or solid tumors comprising the administration of a therapeutically effective amount of catechins, a group of polyphenols found in green tea, to a mammal in need of such therapy. Compositions of catechins include but not limited to, **epigallocatechin gallate** (EGCg), epicatechin (EC), **epicatechin gallate** (ECG), epigallocatechin (EGC). The unique compositions of the invention contain various **combinations** of the catechins, alone or in **combination** with each other or other therapeutic agents and are used to treat primary and metastatic cancers in humans. The invention also encompasses the varying modes of administration of the therapeutic compounds.

ACCESSION NUMBER: 2002:152242 USPATFULL
TITLE: Tea catechins as cancer specific proliferation inhibitors
INVENTOR(S): Morre , Dorothy M., West Lafayette, IN, United States
Morre , James D., West Lafayette, IN, United States
PATENT ASSIGNEE(S): Purdue Research Foundation, West Lafayette, IN, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6410061	B1	20020625	
APPLICATION INFO.:	US 2000-537211		20000329	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-151109P	19990827	(60)
	US 1999-126893P	19990330	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Tate, Christopher R.
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 28 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 1977
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention described herein encompasses a methods and compositions of treating cancer or solid tumors comprising the administration of a therapeutically effective amount of catechins, a group of polyphenols found in green tea, to a mammal in need of such therapy. Compositions of catechins include but not limited to, **epigallocatechin gallate** (EGCg), epicatechin (EC), **epicatechin gallate** (ECG), epigallocatechin (EGC). The unique compositions of the invention contain various **combinations** of the catechins, alone or in **combination** with each other or other therapeutic agents and are used to treat primary and metastatic cancers in humans. The invention also encompasses the varying modes of administration of the therapeutic compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

6 ANSWER 9 OF 206 USPATFULL

ACCESSION NUMBER:	2001:226668 USPATFULL
TITLE:	Histidine containing nutriceutical
INVENTOR(S):	Thomas, Peter G., Charlottesville, VA, United States Wade, A. Michael, Mebane, NC, United States
PATENT ASSIGNEE(S):	Cytos Pharmaceuticals LLC, Durham, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6329414	B1	20011211
APPLICATION INFO.:	US 1999-393891		19990910 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1997-962655, filed on 3 Nov 1997, now patented, Pat. No. US 5972985		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Jarvis, William R. A.		
LEGAL REPRESENTATIVE:	Angres, Isaac, Petraglia, Susan		
NUMBER OF CLAIMS:	3		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1128		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Nutriceutical compositions useful as a dietary supplement which have antioxidant/free radical scavengers and also having a cytoprotective effect are disclosed. The compositions contain a cytoprotective and antioxidant/free radical scavenging amount of at least one of D-histidine, L-histidine, a racemic mixture thereof, a non-racemic mixture thereof, and nutriceutically acceptable salts thereof in **combination** with phytonutrients having antioxidant properties such as canthanaxin, vitamin A and limonene. The compositions can be prepared in **capsule** form, **tablets**, sustained release **tablets**, **suspensions** and **oral** rehydration **solutions**.

ACCESSION NUMBER: 1998:243887 CAPLUS
DOCUMENT NUMBER: 129:27274
TITLE: Antioxidant synergism of tea polyphenols and .alpha.-tocopherol against free radical induced peroxidation of linoleic acid in **solution**
AUTHOR(S): Jia, Zhi-Sheng; Zhou, Bo; Yang, Li; Wu, Long-Min; Liu, Zhong-Li
CORPORATE SOURCE: National Laboratory Applied Organic Chemistry, Lanzhou University, Lanzhou, 730000, Peop. Rep. China
SOURCE: Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1998), (4), 911-915
CODEN: JCPKBH; ISSN: 0300-9580
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peroxidn. of linoleic acid was initiated by a water sol. azo initiator 2,2'-azo(2-amidinopropane)-dihydrochloride (AAPH) in tert-Bu alc.-water **soln**. and inhibited by .alpha.-tocopherol and polyphenols extd. from green tea, i.e. (-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-**epicatechin gallate** (ECG), (-)-**epigallocatechin gallate** (EGCG) and gallic acid (GA), either alone or in **combination**. The reaction kinetics were followed by oxygen uptake, formation of linoleic acid hydroperoxides and consumption of the antioxidants. It was found that the tea polyphenols could slow the rate of peroxidn. with an activity sequence of EGCG > EGC .apprx. ECG > EC .apprx. GA, but no definite inhibition period was obsd. On the other hand, the tea polyphenols could significantly increase the inhibition period of .alpha.-tocopherol and protect the latter from depletion with an activity sequence of EGCG >> ECG .apprx. EGC > GA > EC when they were used in **combination**. A **synergistic** antioxidn. mechanism involving the recycling of .alpha.-tocopherol by the tea polyphenol is proposed.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CCESSION NUMBER: 2000:706979 CAPLUS
DOCUMENT NUMBER: 133:286469
TITLE: Compositions containing tea catechins as cancer specific proliferation inhibitors
INVENTOR(S): Morre, Dorothy M.; Moore, D. James
PATENT ASSIGNEE(S): Purdue Research Foundation, USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057875	A1	20001005	WO 2000-US8332	20000329

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-126893P P 19990330
US 1999-151109P P 19990827

AB The invention described herein encompasses method and compns. of treating cancer of solid tumors comprising the administration of a therapeutically effective amt. of catechins, a group of polyphenols found in green tea, to a mammal in need of such therapy. Compns. of catechins include but not limited to, **epigallocatechin gallate** (EGCg), epicatechin (EC), **epicatechin gallate** (ECG), epigallocatechin (EGC). The unique compns. of the invention contain various **combinations** of the catechins, alone or in **combination** with each other or other therapeutic agents and are used to treat primary and metastatic cancers in humans. The invention also encompasses the varying modes of administration of the therapeutic compds. EGCg was inhibited NADH oxidase activities in plasma membranes from human mammary adenocarcinoma (BT-20) and HeLa (human cervical carcinoma) cells.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT